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Original Research Article

A study of Association between Thyroid Profile and Glycated Haemoglobin in Patients with Type II Diabetes Mellitus

Dr. Aruna Tushar Sharma[1], Dr. Gaurang Kishorbhai A[2*], Dr. N. Haridas[3]
[1]Tutor, Department of Biochemistry, Dr. M K Shah Medical College and Research Institute, Ahmedabad-Gujarat, India
[2]Assistant Professor, Department of Biochemistry, Dr. M K Shah Medical College and Research Institute, Ahmedabad-Gujarat, India
[3]Professor & Head, Department of Biochemistry, Dr. N. D. Desai Medical College, Nadiad-Gujarat, India

***Corresponding author:** Dr. Gaurang Kishorbhai A
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Abstract

Diabetes mellitus and thyroid diseases are the two most common endocrinopathies encountered in clinical practice. Thyroid hormone abnormalities are frequently associated with diabetes and remain unidentified. Thyroid dysfunction could negatively impact Diabetes and its complications. Thyroid hormone replacement is associated with a decrease in Glycated Hemoglobin (HbA1c) level. The present study was undertaken to study association between thyroid profile and glycated Haemoglobin (HbA1c) in Type 2 Diabetes Mellitus patients. A case control study was done at Shri Krishna Hospital in Karamsad city .100 cases of Type 2 Diabetes mellitus and 100 healthy controls were taken. Blood samples were collected and analyzed for thyroid profile, HbA1c, Fasting Blood Sugar and Renal Function Test. We found that there was a positive correlation between TSH (Thyroid stimulating hormone) and HbA1c levels, and a negative correlation between Thyroid hormones [Triiodothyronine (T_3) & Thyroxine (T_4)] and Glycated Haemoglobin (HbA1c) in cases of type 2 Diabetes Mellitus. There is a significant decrease in TT_3 (Total Triiodothyronine) and TT_4 (Total Thyroxine) and significantly increased TSH in cases of Diabetes mellitus as compare to healthy Controls. We found that out of 100 cases of type 2 Diabetes Mellitus, 31% patients showed thyroid disorders. There is a high prevalence of thyroid disorders in Diabetic patients. If not diagnosed early, it could negatively affect diabetes and its complications. Therefore, routine screening of thyroid profile in diabetic patients is advisable to improve quality of life and reduce morbidity rate.

Keywords: Thyroid profile, Glycated Hemoglobin (HbA1c), Type 2 Diabetes Mellitus.

INTRODUCTION

Diabetes mellitus is a global health problem affecting major populations worldwide. It is a group of metabolic disorders characterized by absolute or relative deficiencies in insulin secretion with chronic hyperglycaemia and disturbances of carbohydrate, lipid, and protein metabolism [1]. Thyroid hormones are secreted from thyroid gland. Upon stimulation by thyroid stimulating hormone (TSH), the thyroid gland responds by producing and releasing two thyroid hormones [2]. Insulin and thyroid hormones are intimately involved in cellular metabolism and thus excess or deficit of either of these hormones result in the functional derangement of the other. One of the important function of thyroid hormones is the regulation of carbohydrate metabolism and pancreatic function and on the other hand, diabetes affects thyroid function tests to variable extents so Diabetes and thyroid disorders have been shown to mutually influence each other and association between both conditions have been reported [3, 4]. Thyroid hormone abnormalities are frequently associated with diabetes and unidentified thyroid dysfunction could negatively impact diabetes and its complications [5]. Thyroid hormone replacement is associated with a decrease in glycated hemoglobin (HbA1c) level, which is influenced by increased erythropoiesis rather than by changes in glucose level [6, 7].

The report showing the association between diabetes and thyroid dysfunction were first published in 1979 [8] stating that prevalence of thyroid dysfunction varied from 2.2%–17% in diabetics. Diabetic women are more frequently affected than men and hypothyroidism is more common than thyrotoxicosis [9]. Glycemic control in diabetic patients is usually monitored by determination of HbA1c levels (glycated haemoglobin) which is now the gold standard, and gives an estimate of the amount of glucose in the blood over the previous three months.

To the best of my knowledge, studies on the association between Thyroid Profile and HbA1c among

the diabetic population in Gujarat are scanty. Therefore, this study is undertaken to provide a comprehensive and comparative study of TT_3 and TT_4, TSH and glycemic control parameter Glycated Haemoglobin [HbA1c] in patients of Type 2 DM.

MATERIALS AND METHODS

Study type, Study setting and Study Period

A hospital based case control study was carried out in Shri Krishna Hospital in Karamsad city of Gujarat from December 2014 to November 2015.

Participants' Recruitment Procedure

100 participants were in the study group and 100 participants in control groups were enrolled by following procedure.

Selection of Study Group

Patients aged 30 years or more who came to Shree Krishna hospital for routine health check-up were taken for the study. Basic information, clinical history was taken from the record files.

Inclusion Criteria

100 type II Diabetes Mellitus patients diagnosed as per American Diabetes Association (ADA)[10] having FPG >126 mg/dl, HbA1c > 6.5%, Serum Urea < 40 mg/dl , Serum Creatinine < 1.3mg/dl were included in the study as cases.

Exclusion Criteria

Non Diabetic individuals, individuals having history of thyroid diseases and taking medicines that affect thyroid function and individuals with Liver or kidney diseases were excluded from the study.

Selection of Control Group:-

Inclusion Criteria

Age and sex matched normal healthy individuals with FPG <110 mg/dl, HbA1c< 6.5%, Serum Urea < 40 mg/dl, Serum Creatinine <1.3mg/dl were included in the study as controls.

Exclusion Criteria

Individuals having history of thyroid diseases and individuals with liver or kidney diseases were excluded from the study.

Blood Sample Collection and Processing

Samples were collected with an aseptic blood collection technique. Three vacutainers: Plain tube for Renal function tests ,TSH, TT_3 and TT_4 .Sodium fluoride tube for Fasting plasma glucose and EDTA tube for HbA1c were taken. These blood samples were processed and analysed in the biochemistry laboratory for the estimation of FPG, HbA1c, TSH, TT_3 and TT_4

Estimation of Plasma Glucose [11]

Fasting Plasma glucose was estimated by Hexokinase method in fully automated Roche Cobas Integra 400 plus clinical chemistry analyser.

Estimation of glycated haemoglobin (HbA1c) [12]

HbA1c was measured by Immunoturbidimetry Standardized method according to IFCC in fully automated Roche Cobas Integra 400 plus clinical chemistry analyser.

Estimation of Total T_3, Total T_4, Thyroid Stimulating Hormone [13]

TT_3 and TT_4, TSH were measured by electro chemiluminescence (ECL) method in Roche Cobas E - 411 Immunoassay Analyser.

In Renal function test, serum creatinine was estimated by Jaffe's kinetic method and Serum urea was estimated by urease method in fully automated Roche Cobas Integra 400 plus clinical chemistry analyser.

Statistical Analysis

Data were entered and analysed through Excel 2007. Categorical variables were expressed through percentages while continuous variables were expressed as mean and standard deviation. Pearson correlation coefficient were calculated to know correlation between thyroid profile [Triiodothyronine (T_3), Thyroxine (T_4), Thyroid Stimulating Hormone (TSH)] and Glycated haemoglobin in cases of Type 2 Diabetes Mellitus.

RESULTS

Table-1 shows that mean age among control groups was lower than the mean age of the case group. Fasting plasma glucose and Glycated haemoglobin were significantly higher (p value <0.05 in both). Mean TSH level were significantly higher in cases while serum Total T3 and Total T4 levels were significantly decreased in cases when compared to controls.

The results of thyroid function were classified on the use of the following as normal reference range:

- **TSH-** 0.40–4.2 mIU/L
- **Total T3-** 1.3-3.1 nmol/L
- **Total T4-** 66-181 nmol/L
- **Hypothyroidism**—when Total T3, Total T4 were less and TSH greater than the reference ranges
- **Hyperthyroidism**—when Total T3, Total T4 were greater and TSH less than the reference ranges
- **Subclinical hypothyroidism**—when Total T3, Total T4 were within normal range and TSH greater than the reference ranges
- **Subclinical hyperthyroidism**—when Total T3, Total T4 were within normal range and TSH less than the reference ranges

Table-1: Comparison of Variables between Cases And Controls

Variables	Cases (n=100) (Mean ± SD)	Controls (n=100) (Mean ± SD)	p value
Age (Years)	55.09 ± 11.03	52.54 ± 9.06	0.06
Gender Female Male	 42 (46.67%) 58 (52.73%)	 48(53.33%) 52(47.27%)	0.48
Fasting Plasma Glucose(FPG) (mg/dl)	165.92 ± 45.86	94.63 ± 9.20	<0.0001**
Glycated haemoglobin (HbA1c) (%)	8.00 ± 1.58	5.65 ± 0.53	<0.05*
Thyroid Stimulating Hormone(TSH) (micro unit/ml)	4.36±2.45	3.32±2.10	<0.05*
Total Triiodothyronine(TT3) (nano mol/litre)	1.65±0.52	2±0.62	<0.05*
Total Thyroxine (TT4) (nano mol/litre)	99.77±30.49	114±31.47	<0.05*

* "p" value less than 0.05 indicates significant value
** "p" value less than 0.001 indicates highly significant value

Table-2: Distribution of Diabetic Subjects with Abnormal Thyroid Profile

Thyroid Disorders	Cases		Controls
	HbA1c <7.5%	HbA1c >7.5%	
Hypothyroidism(Primary)	3	9	2
Hypothyroidism(Subclinical)	4	13	2
Hyperthyroidism(Primary)	0	1	0
Hyperthyroidism(Subclinical)	0	1	1
Total	07	24	5

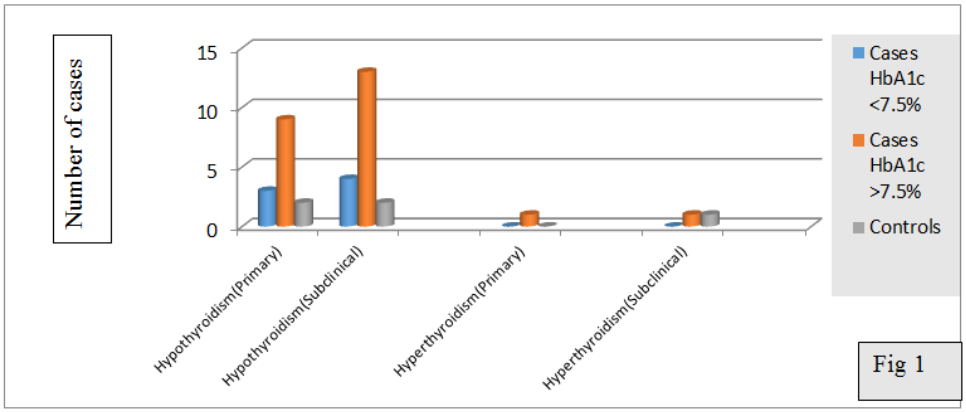

Fig-1: Categorical comparison of thyroid Diseases among type 2 Diabetes Mellitus having HbA1c < 7.5 %, HbA1c > 7.5 % and Healthy controls

Table-3: Correlation of Thyroid Profile with HbA1c

Parameters	Correlation Coefficient	p value
HbA1c – Thyroid Stimulating Hormone(TSH)	0.64	<0.001**
HbA1c – Total Triiodothyronine(TT_3)	-0.38	<0.001**
HbA1c –Total Thyroxine (TT_4)	-0.33	<0.001**

** "p" value less than 0.001 indicates highly significant value

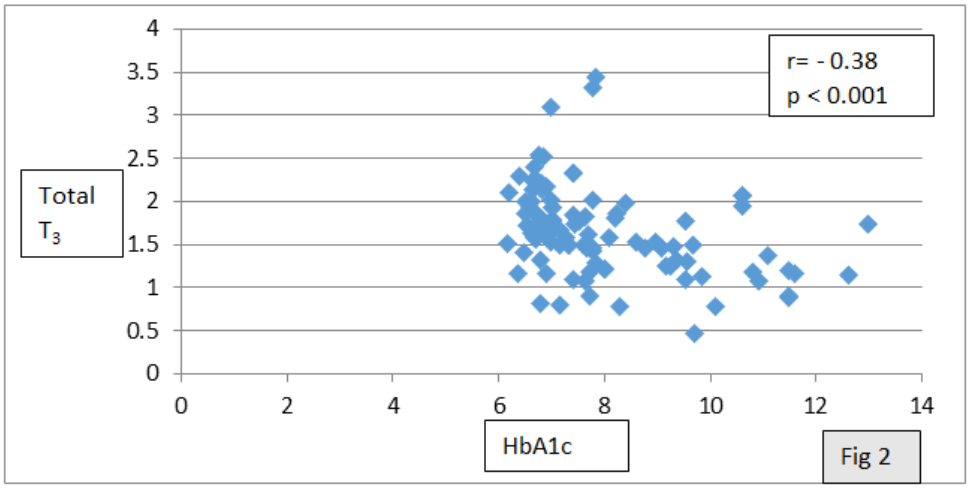

Fig-2: Scatter Diagram showing association between HbA1c and T_3

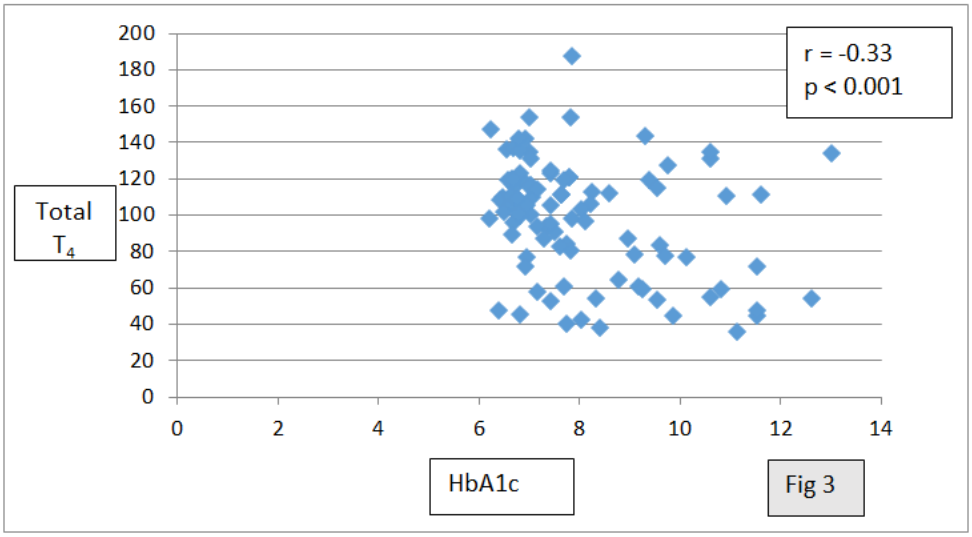

Fig-3: Scatter Diagram showing association between HbA1c and Total T_4

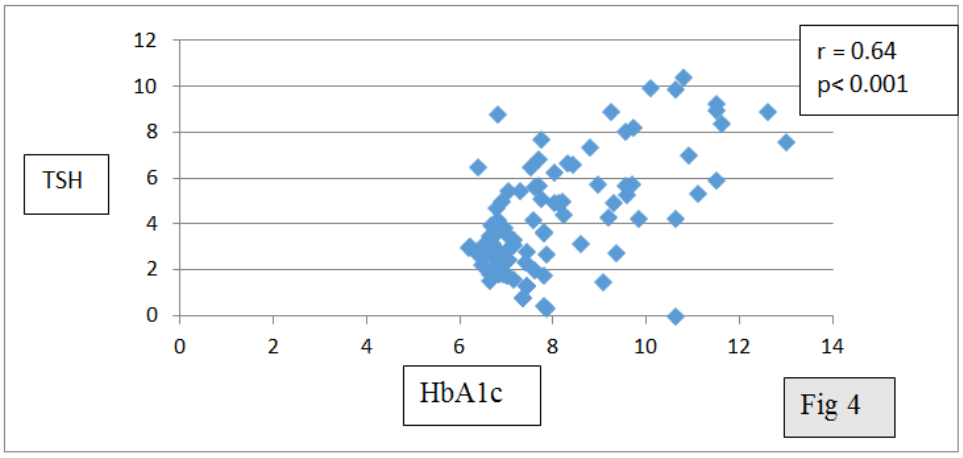

Fig-4: Scatter Diagram showing association between HbA1c and TSH

DISCUSSION

In our case control study, done over a period of one year from December 2014 to November 2015. 100 cases of Type 2 Diabetes Mellitus and 100 healthy controls were included in the study.

The results of our study showed that the levels of Total T3, Total T4 were significantly lower in diabetic patients as compare to controls and serum TSH was significantly higher in diabetics as compared to controls [See Table-1]. This is in accordance with the

studies of Vikram BV *et al*., [14], Gurjeet S *et al*., [15] and Shekhar CY *et al*., [16]. Altered thyroid hormones have been described in patients with diabetes especially those with poor glycemic control because of alterations in the hypothalamo-pituitary-thyroid axis. In diabetic patients, the nocturnal TSH peak is blunted or abolished, and Response of TSH to TRH is also decreased [17]. Production of T3, T4 and iodide uptake by thyroid gland is diminished. In addition to these, deiodination of T4 to T3 is decreased which explains reduction in T3 and T4 level in serum [18].

In our study among the 100 diabetic subjects, investigated 12 % i.e.12 had hypothyroidism, 17% i.e.17 had subclinical hypothyroidism, 1% i.e.,1 had subclinical hyperthyroidism so total of 31% patients showed thyroid disorder. We also found that 5 % i.e. 5 of the healthy control subjects had abnormal thyroid status [See Table-2 and Fig-1]**.** In Fig-1, Bar Graph also suggests that HbA1c levels more than 7.5 % have the tallest bar representing Thyroid disorders These findings suggest a high prevalence of thyroid disorders in diabetic population specially in uncontrolled Diabetes which is supported by the studies of Celani et al.(Prevalence rate -31.4%)[19], Smithson (Prevalence rate -10.4%) [20]. Radaideh *et al*., (Prevalence rate - 12.5%) [21], Pimenta *et al*., (Prevalence rate -51.6%) [22], Udiong *et al*., (Prevalence rate - 46.5%) [23].

In cases of type 2 Diabetes Mellitus, there was a positive correlation between TSH (correlation coefficient is 0.64, p value is < 0.001)and HbA1c. There was a negative or inverse correlation between HbA1c level and Total Triiodothyronine (Total T_3) (correlation coefficient is -0.38, p value is < 0.001), there was also negative or inverse correlation between HbA1c level Total Thyroxine (Total T_4) (correlation coefficient is -0.33, p value is < 0.001) [See Table-3 and Fig 2-4]. The observation of negative correlation between T3 and HbA1c is supported by the studies of Schlienger JL *et al*., Bagchi N, [24, 25]. It has recently been reported that T3 has an anti-apoptotic and protective effect on the pancreatic beta cells [15]. T3 activates the PI-3 kinase pathway via thyroid hormone receptor on the beta cell, and stimulates insulin secretion. This may be related to an association between low Total T3 levels, and increased HbA1c [26, 27]. The observation of positive correlation between TSH and HbA1c is supported by the studies of Velija-Asimi *et al*., [28]. They examined the effects of treatment of subclinical hypothyroidism and concluded that the correlation between TSH and HbA1c were positive and significant.

CONCLUSION

The present study revealed that patients with Type 2 Diabetes Mellitus have higher prevalence of thyroid disorders. The most common thyroid disorder found in type 2 Diabetes Mellitus is hypothyroidism. In thyroid disorders, early signs and symptoms of underlying disease remain hidden. Also, most of the times undiagnosed thyroid disorders could negatively affect Diabetes and its complications. Therefore, routine screening of thyroid profile in diabetic patients is beneficial and advisable to improve quality of life and reduce morbidity rates and its complications.

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